2

Hazard Identification

Escherichia coli O157:H7, a Shiga toxin-producing *E. coli,* was first recognized as a human pathogen in 1982, when it was associated with two outbreaks of hemorrhagic colitis (bloody diarrhea). The outbreaks occurred in Oregon and Michigan and involved the consumption of hamburgers from a fast-food chain (Riley et al. 1983). The spectrum of infection with *E. coli* O157:H7 includes asymptomatic fecal shedding of the organism; nonbloody or bloody diarrhea accompanied by abdominal cramps, vomiting, and occasionally fever; postdiarrheal hemolytic uremic syndrome (HUS); and thrombotic thrombocytopenic purpura (TTP). The continued occurrence of widespread outbreaks and an increase in the incidence of reported cases have led to the designation of *E. coli* O157:H7 as an emerging pathogen. Since 1982, epidemiologic studies have shown that *E. coli* O157:H7 can be transmitted through water (by drinking or swimming in contaminated water), food, or person-to-person contact, especially in a daycare setting. Ground beef continues to be a significant source of *E. coli* O157:H7 infection in humans. This chapter on hazard identification begins with a discussion of the importance of *E. coli* O157:H7 in the context of other Shiga toxin-producing *E. coli*. The chapter then discusses the sources of *E. coli* O157:H7; its epidemiology, including the types of food and risk factors associated with infection; adverse health outcomes; and the organism's pathogenesis. The factors that contribute to the growth and persistence of *E. coli* O157:H7 in the environment are then discussed.

ESCHERICHIA COLI

Multiple genetic subtypes of *E. coli* exist; many are part of the normal mammalian intestinal flora and do not cause disease in humans. *E. coli* strains that cause diarrheal illness are categorized into specific groups on the basis of virulence properties, mechanisms of pathogenicity, and clinical syndromes. These categories include enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), enteroinvasive *E. coli* (EIEC), diffuse-adhering *E. coli* (DAEC), enteroaggregative *E. coli* (EaggEC), and Shiga toxin-producing *E. coli* (STEC). *E. coli*

O157:H7 is in the STEC group and can produce Shiga toxin 1, Shiga toxin 2, or both. Shiga toxin production alone may not be enough to cause illness. In addition to Shiga toxin, some strains of STEC contain genes that code for the ability to attach and damage intestinal tract cells, causing what is commonly referred to as attaching and effacing lesions. When a STEC has the full complement of these virulence genes and has been associated with an illness such as bloody diarrhea, it is often referred to as enterohemorrhagic *E. coli* (EHEC).

E. coli O157:H7 are easily differentiated biochemically from other enteric *E. coli* because they ferment sorbitol slowly, whereas other *E. coli* usually readily ferment sorbitol. Since the organism's first recognition as a human pathogen in 1982, diagnostic screening assays that capitalize on this difference have become widely used in clinical laboratories (Wells et al. 1983). This practice has resulted in the generation of much more information on *E. coli* O157:H7 than that available on non-O157 STEC.

The ability to detect *E. coli* O157:H7 in laboratory samples has recently been improved by the development of a separation technique that uses immunomagnetic beads. In this method, microscopic, iron cored beads are coated with antibody specific to *E. coli* O157:H7 (Okrend et al. 1992). The antibody coated beads capture *E. coli* O157:H7 organisms, and in turn, the bead-cell complexes are captured using a magnetic concentrator. These complexes can then be removed from the sample and plated onto MacConkey sorbitol agar for culture and isolation of *E. coli* O157:H7. This method has been especially useful for samples that have potentially large numbers of background organisms, such as meat products and feces, in which the growth of other bacterial species can obscure *E. coli* O157:H7 colonies during culture.

In the United States, several outbreaks have occurred from exposure to non-O157 STEC. In Montana, 18 persons developed bloody diarrhea in 1994 after exposure to contaminated milk; *E. coli* O104:H21 was cultured from the stools of three of these patients (CDC 1995). *E. coli* O111:H8 was responsible for an outbreak of gastrointestinal illness, including bloody diarrhea, in 56 persons who attended a camp in Texas in 2000 (CDC 2000a). Non-O157 serotypes of *E. coli*, including O26:H11, O111:H8, O103:H2, O113:H21, and O104:H21, have been responsible for a few outbreaks throughout the world. In a cluster of three cases of HUS caused by O113:H21 in Australia, this organism was found not to have genes coding for attaching and effacing (Paton et al. 1999).

A recent Nebraska study of stool samples from persons with a differential diagnosis of bacterial gastroenteritis found 6 (1.8%) of 335 samples positive for *E. coli* O157:H7, whereas 8 samples were positive for non-O157 STEC (Fey et al. 2000). In Washington state, a 1-year prospective study tested 445 stool samples from children who had diarrhea and isolated a non-O157 STEC from 13 (1.1%) patients and *E. coli* O157:H7 from 5 (2.9%) patients (Bokete et al. 1993). A national study of postdiarrheal HUS estimated that less than 20% of HUS cases were due to non-O157 STEC; however, the authors qualified that estimate, commenting that it was difficult to determine the proportion of STEC-associated HUS that resulted from non-O157 STEC (Banatvala et al. 2001).

Most clinical laboratories in the United States do not routinely screen for non-O157 STEC because of the lack of a biochemical marker (Mead and Griffin 1998). In addition, surveillance for cases of non-O157 STEC infection is not routinely conducted. Mead et al. (1999) estimated that the incidence of non-O157 STEC is 20% to 50% that of *E. coli* O157:H7 infection. Therefore, because *E. coli* O157:H7 is the most important STEC serotype in the United States in terms of public health and because of the current paucity of epidemiologic data for non-O157 STEC, this risk assessment is limited to *E. coli* O157:H7.

SOURCES OF *E. COLI* O157:H7

E. coli O157:H7 has been isolated from the feces or gastrointestinal tract of cattle, sheep, horses, pigs, turkeys, dogs, and a variety of wild animal species (Kudva et al. 1996; Rice and Hancock 1995; Hancock et al. 1998b; Heuvelink et al. 1999); however, epidemiologic studies have found that cattle manure is the source of most human *E. coli* O157:H7 infections. *E. coli* O157:H7 has also been isolated from bodies of water (e.g., ponds, streams), wells, and water troughs and has been found to survive for months in manure and water trough sediments (Wang and Doyle 1998; Hancock et al. 1998a; Kudva et al. 1998; Sargeant et al. 2000).

Colonization of the gastrointestinal tract for longer than 2 or 3 months has not been reported in any species, although only cattle, sheep, and humans have been sampled with sufficient intensity to assess duration of carriage (Hancock et al. 1998a). Despite this finding, *E. coli* O157:H7 has been described as "ubiquitous" in dairy and beef cattle and is present at least occasionally on most farms or feedlots (Hancock et al. 1998a; Hancock et al. 2001). This widespread prevalence in cattle has been attributed to the organism's ability to survive for at least 4 months in water trough sediments, providing an ongoing source of exposure to cattle (Hancock et al. 1998a). *E. coli* O157:H7 is also present in purchased animal feeds; therefore, such feeds may be an important route by which *E.* coli O157:H7 is disseminated to farms (Hancock et al. 2001). From the farms, *E. coli* O157:H7 contamination of meat occurs when beef carcasses come into contact with hides and feces during the slaughter process (Elder et al. 2000).

EPIDEMIOLOGY OF DISEASE DUE TO INFECTION WITH *E. COLI* O157:H7

E. coli O157:H7 was designated by the Council of State and Territorial Epidemiologists as a nationally notifiable disease in 1994. From 1994 to 2000, the number of reported cases of *E. coli* O157:H7 in the United States increased by 211%, from 1,420 (0.8 per 100,000 population) in 1994 to 4,410 (approximately 1.6 per 100,000 population) in 2000 (CDC 1999a; CDC 2001b) (Figure 2-1). Cases are reported by passive surveillance through the National Notifiable Diseases Surveillance System (NNDSS). Health care providers use this system to report notifiable disease cases to local or state health departments. The increase in reported cases over time is probably due to a combination of factors including (1) improvement in the effectiveness of the surveillance system; (2) greater awareness of *E. coli* O157:H7 infection among health care providers and the public, which has led to improved detection and reporting; (3) enhanced ability to detect disease through better diagnostic tests; and (4) a true increase in the incidence of disease.

In 1996, the Emerging Infections Program, Foodborne Diseases Active Surveillance Network (FoodNet) began a program of active surveillance of clinical laboratories for specific foodborne diseases, including *E. coli* O157:H7. Five states participated initially (Minnesota, Oregon, and selected counties of California, Connecticut, and Georgia); as of 2000, eight states were under active surveillance, representing 29.5 million persons (10.8% of the 1999 U.S. population) (CDC 2001a). The number of cases of *E. coli* O157:H7 infection reported annually to FoodNet ranged from 388 in 1996 to 631 in 2000 (Bender et al. 2000; CDC 2000c; CDC 2001a). Because the population under surveillance has increased, it is more appropriate to compare the number of reported cases per 100,000 population. For 1996 to 2000, there were 2.7, 2.3, 2.8, 2.1, and 2.9 reported cases per 100,000 population, respectively, for the five original states (CDC 2001a). Data on the prevalence of symptomatic *E. coli* O157:H7 infection prior to the inception of FoodNet are scarce. Ostroff et al. (1989) reported an incidence of 2 cases per 100,000

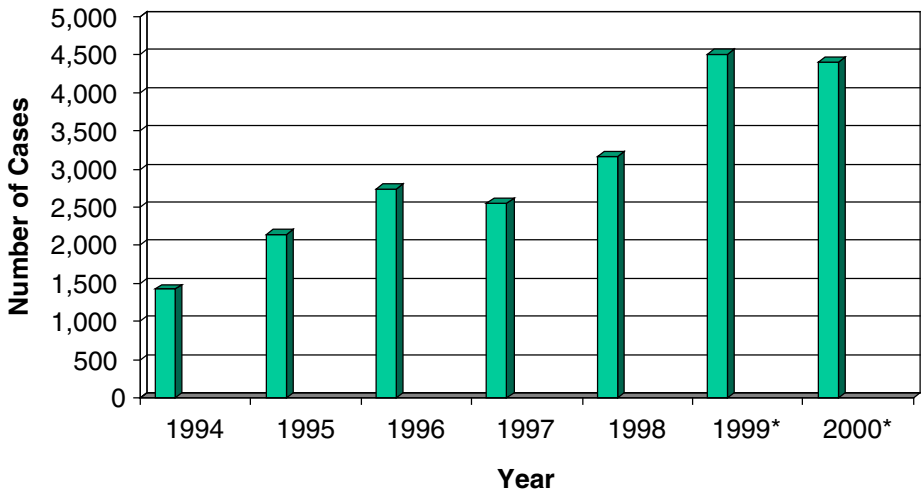

FIGURE 2-1 Number of reported cases of *E. coli* O157:H7 infection, United States, 1994–2000. *Provisional. Sources: CDC, NNDSS.

population during the first year of statewide surveillance in Washington in 1987. A prospective, population-based study, also conducted in Washington, estimated the incidence of culture-confirmed *E. coli* O157:H7 infection to be 8 per 100,000 enrollees in a Seattle-based health maintenance organization during 1985 to 1986 and 10 per 100,000 enrollees in 1987 (MacDonald et al. 1988; Ostroff et al. 1989). The results of this latter study may provide a more accurate estimate of the incidence of *E. coli* O157:H7 infection and suggest that substantial underreporting occurred in the statewide passive surveillance program.

The incidence of *E. coli* O157:H7 infection varies by age group, with the highest incidence of reported cases occurring in children. In 1998, the incidence in children younger than 1 year of age was 2.01 per 100,000 population. The highest incidence was found in 1- to 4-year-olds at 4.57 reported cases per 100,000 population, whereas 5- to 14-year-olds had an incidence of 1.83 reported cases per 100,000 population (CDC 1999a). The lowest incidence occurred in persons aged 15 or older and ranged from 1.15 to 0.61 reported cases per 100,000 population. At FoodNet sites in 1999, 35.3% of reported cases occurred in 1- to 10-year-olds, 17.6% of cases occurred in 10- to 20-year-olds, and 14.1% of cases occurred in persons older than 60 (CDC 2000b). Other studies have also found a high incidence in children (Ostroff et al. 1989; Proctor and Davis 2000).

Diagnosis of *E. coli* O157:H7 is more common in the summer months (Mead and Griffin 1998). Of cases reported by FoodNet sites, 70% occurred during June through September for the years 1996 to 1998 (Bender et al. 2000). In 1998, 1,710 (54.1%) of 3,161 cases of *E. coli* O157:H7 reported through NNDSS to CDC occurred during those months (CDC 1999a). Outbreaks also occur more frequently in the summer, with 50 (58.8%) of 85 foodborne outbreaks occurring during June through September for the period 1993 to 1997 (CDC 1999a). During 1998 to 1999, 21 (50.0%) of 42 foodborne outbreaks occurred during June through September (CDC 2000c; CDC 2001c).

Most postdiarrheal HUS cases are thought to be due to *E.* coli O157:H7 infection. In a study of 83 patients infected with HUS between 1987 and 1991, STEC was implicated as the cause of illness in 72% of the patients; more than 80% of these cases were caused by *E. coli* O157:H7 infection (Banatvala et al. 2001). Siegler et al. (1994) found that 140 (89.2%) of 157 HUS cases that occurred in Utah between 1971 and 1990 were postdiarrheal. *E. coli* O157:H7 testing was only available for the last 4 years of this study, but the authors concluded that *E. coli* O157:H7

may have been the leading cause of HUS in that region of the United States for the duration of the study period (Siegler et al. 1994).

HUS has been a nationally notifiable disease since 1996, and cases are reported by passive surveillance through NNDSS. Active surveillance for HUS in children at FoodNet sites began in 1997. In 1998, the most recent year for which data are available, 90 cases of HUS were reported through NNDSS (CDC 1999a). In 1999, 60 cases were reported and 8 (13.3%) deaths occurred at FoodNet sites (CDC 2000b). HUS occurs more commonly in children than adults. During 1997 to 1999 at FoodNet sites, the overall incidence of HUS among children younger than 15 years of age was 0.7 per 100,000 population; for children younger than 5, the incidence was 1.4 per 100,000 (CDC 2000b). In a nationwide study of 83 patients with HUS, 46 (55.4%) were younger than 5 years old and an additional 27 (32.5%) were 5 to 17 years old (Banatvala et al. 2001).

Similar to the seasonal distribution in reported cases of *E. coli* O157:H7 infection, HUS cases occur more frequently in summer months. In 1998 and 1999, respectively, 31 (59.6%) of 52 reported HUS cases and 41 (68.3%) of 60 cases in the United States occurred during June through September (CDC 1999a; CDC 2000b). Additional details about HUS can be found in the section below on adverse health outcomes associated with *E. coli* O157:H7 infection.

The number of reported *E. coli* O157:H7 cases derived from surveillance is known to be an underestimate of the true disease burden. Underestimation of the actual incidence of infection occurs for a variety of reasons:

- Some infected persons do not seek medical care.
- Physicians do not perform diagnostic testing on all patients who have symptoms of infection.
- Some persons who obtain medical care do not provide a stool specimen.
- Laboratories do not culture all stool samples for *E. coli* O157:H7.
- Some proportion of laboratory results are false negatives.
- Not all culture-confirmed infections are reported to public health authorities by health care providers and laboratories.

For example, in a 1994 national survey, 70 (54.3%) of 129 randomly selected clinical laboratories reported that they did not routinely test all stools or all bloody stools for *E. coli* O157:H7 (Boyce et al. 1995b). However, routine culturing of bloody diarrhea for *E. coli* O157:H7 is increasingly common, particularly in FoodNet sentinel site areas. Using surveillance data and accounting for the factors that contribute to underreporting, Mead et al. (1999) estimated that 73,480 cases of *E. coli* O157:H7 infection occur annually in the United States and that 85% (62,456 cases) are a result of foodborne exposure.

TRANSMISSION OF *E. COLI* O157:H7

To choose the most appropriate product to model in this risk assessment, we assessed how frequently various products were implicated in *E. coli* O157:H7 infection by evaluating studies of sporadic cases of *E. coli* O157:H7 infection and outbreak investigation reports. Sporadic cases account for the majority of reported cases in a given year and therefore may be more representative of persons with *E. coli* O157:H7 infection. For example, 75% of reported cases in Oregon during 1991 to 1997 and 83% of reported cases in Wisconsin during 1992 to 1999 were sporadic (OCD 1998; Proctor and Davis 2000).

In the first nationwide case-control study of sporadic *E. coli* O157:H7 infection, conducted in 1990 to 1992, consumption of undercooked ground beef (described as “pink in the middle”) was the only dietary factor independently associated with diarrhea in multivariate analysis. The

population-attributable risk for this behavior was 34% (Slutsker et al. 1998). A study of sporadic cases of *E. coli* O157:H7 infection in New Jersey found that these individuals were more likely than healthy controls to have eaten a hamburger in the week preceding illness (Mead et al. 1997). In addition, patients were slightly more likely than controls to report having eaten a hamburger that was pink in the middle (45% vs. 33%) (Mead et al. 1997). Kassenborg et al. (2001) also found that consumption of pink hamburgers or pink ground beef was a statistically significant risk factor, although merely consuming ground beef was not. Other significant risk factors by multivariate analysis were exposure to farms or to cattle, eating at a table service restaurant, using immune suppressive medication (for adults only), and obtaining beef through a private slaughter arrangement. This study estimated the population-attributable risk from consuming pink hamburger was 8% for meals consumed at home and 7% for meals consumed away from home and was 18% for farm exposures (visiting or living on a farm) (Kassenborg et al. 2001).

A prospective study in Washington state identified that rare ground beef was consumed more often by cases than controls (MacDonald et al. 1988). A Canadian study of sporadic cases conducted in 1990 identified consumption of undercooked ground beef as a risk factor for *E. coli* O157:H7 infection; the attributable risk was 17% (Le Saux et al. 1993). In a case-control study of sporadic cases conducted in Oregon during 1996 to 1997, visiting or living on a farm where cattle were present was a risk factor associated with *E. coli* O157:H7 infection (OCD 1998).

Outbreak investigations have contributed significantly to our understanding of how *E. coli* O157:H7 is transmitted. Since the first recognized ground beef-associated outbreak in 1982 (Riley et al. 1983), outbreaks have been attributed to foodborne, waterborne, and person-to-person means of transmission. In 13 outbreaks that occurred between 1982 and 1993 in the United States, the transmission source was identified as hamburger or ground beef in 7 (53.9%) (Griffin 1995).

A total of 128 foodborne outbreaks due to *E. coli* O157:H7 infection were reported in the United States between 1993 and 1999; of these, the food vehicle was identified in 92 (71.9%) (CDC 1999b; CDC 2000c; CDC 2001c). These 92 outbreaks involved 4,421 cases, with a range of 324 to 1,340 cases per year attributable to outbreaks. Beef was the food item most frequently associated with outbreaks. Of the 92 outbreaks with an identified food vehicle, 42 (45.7%) were attributed to exposure to beef. The specific beef product was not identified for 1993 to 1997 outbreaks, but for the 21 beef-associated outbreaks that occurred during 1998 to 1999, ground beef or hamburger was identified as the vehicle in 19. Two outbreaks in 1999 were attributed to roast beef, and one of these was a result of environmental contamination from manure in a pasture where a picnic was held. A list of food vehicles implicated during 1998 to 1999 outbreaks is shown in Table 2-1. Of the 19 ground beef/hamburger-associated outbreaks, 5 (26.3%) occurred in multiple states.

In summary, individuals can be exposed to *E. coli* O157:H7 in many ways. Current data based both on outbreaks and on sporadic infections indicate that consumption of ground beef is the primary source of *E. coli* O157:H7 exposure. For these reasons, ground beef is the focus of this *E. coli* O157:H7 risk assessment.

ADVERSE HEALTH OUTCOMES ASSOCIATED WITH *E. COLI* O157:H7

Ingestion of *E. coli* O157:H7 results in a wide range of possible outcomes, from asymptomatic infection to death. To cause disease, the *E. coli* O157:H7 must survive acidic conditions within the stomach before moving to distal portions of the gastrointestinal tract. Disease due to *E. coli*

TABLE 2-1 Food Vehicles Implicated in Outbreaks of *E. coli* O157:H7, United States, 1998–1999

Vehicle	1998	1999	Total
Ground beef/hamburger	10	9	19
Roast beef	0	2	2
Lettuce	1	3	4
Coleslaw	2	1	3
Salad	1	1	2
Milk	2	0	2
Tacos	0	1	1
Apple cider	0	1	1
Game meat	0	1	1
Cake	1	0	1
Cheese curd	1	0	1
Fruit salad	1	0	1
Macaroni salad	1	0	1
Multiple	1	0	1
Unknown	0	2	2
Total	21	21	42

Sources: CDC 1999b; CDC 2001c.

O157:H7 occurs primarily in the colon. The incubation period from the time of ingestion to the first symptoms ranges from 1 to 8 days. Asymptomatic shedding of *E. coli* O157:H7 has been documented (Swerdlow and Griffin 1997); however, the proportion of exposed individuals who shed *E. coli* O157:H7 but do not develop symptoms is unknown. Typically the illness begins with abdominal cramps and nonbloody diarrhea, which can, but does not necessarily, progress to bloody diarrhea within 2 to 3 days (Griffin 1995; Mead and Griffin 1998). More severe manifestations of *E. coli* O157:H7 infection include hemorrhagic colitis (grossly bloody diarrhea), HUS (a combination of renal failure, low platelet counts, and hemolytic anemia), and occasionally TTP. Approximately 30% to 45% of patients are hospitalized (Ostroff et al. 1989; Le Saux et al. 1993; Bell et al. 1994; Slutsker et al. 1998). Of the 631 cases reported to FoodNet sites in 1999, 39% were hospitalized (CDC 2000c). Treatment for the more serious manifestations of *E. coli* O157:H7 infection is supportive, and the use of antimicrobial agents has been debated (Mead and Griffin 1998).

Of symptomatic patients, 70% or more usually develop bloody diarrhea (Mead and Griffin 1998). A total of 451 (90.0%) of 501 cases, most of whom were stool culture positive for *E. coli* O157:H7, developed bloody diarrhea during a large outbreak in four western states in 1993 (Bell et al. 1994). In a study of sporadic cases in Washington state, 84 (95.5%) of 88 cases developed bloody diarrhea (Ostroff et al. 1989). However, patients with bloody diarrhea are more likely to seek medical attention, so these estimates may be subject to ascertainment bias. Symptoms of hemorrhagic colitis include severe abdominal cramps followed by grossly bloody diarrhea and edema (swelling), erosion, or hemorrhage of the mucosal lining of the colon (Su and Brandt 1995). Hemorrhagic colitis may be the only manifestation of *E. coli* O157:H7 infection, or it may precede development of HUS. Complications from hemorrhagic colitis associated with *E. coli* O157:H7 include upper-gastrointestinal bleeding and stroke (Su and Brandt 1995). Roberts et al. (1998, citing Boyce et al. 1995a; Ryan et al. 1986) estimate the mortality rate of those suffering hemorrhagic colitis without progression to HUS to be 1%, although Griffin (personal communication) believes that this rate is too high.

The proportion of all patients who develop HUS following *E. coli* O157:H7 infection varies among sporadic cases and outbreak-associated cases. Between 3% and 7% of sporadic cases and 20% or more of outbreak-associated cases of *E. coli* O157:H7 infection will progress to HUS (Mead and Griffin 1998). The proportion of patients who develop HUS following *E. coli* O157:H7 infection is influenced by a variety of factors, including age, bloody diarrhea, fever, elevated leukocyte count, and toxin type (Griffin 1995). Wong et al. (2000) found that 10 (14.1%) of 71 children with *E. coli* O157:H7 infection developed HUS.

HUS is the most common cause of acute renal failure in young children, yet it also has long-term complications. Siegler et al. (1994) found that HUS causes chronic renal sequelae, usually mild, in 51% of survivors (48% of all cases). Neurologic complications occur in about 25% of HUS patients (Mead and Griffin 1998). Neurologic symptoms are generally mild, but serious complications, such as seizure, stroke, and coma, can occur (Su and Brandt 1995). Similar to treatment for *E. coli* O157:H7 infection, only symptomatic treatment is available for neurologic complications, making this manifestation of HUS especially dangerous and an important cause of death in HUS patients. Other complications of HUS include pancreatitis, diabetes mellitus, and pleural and pericardial effusions (Mead and Griffin 1998). In a nationwide study of HUS patients, 46 (55%) of 83 patients required either peritoneal dialysis or hemodialysis during the acute phase of their illness (Banatvala et al. 2001). Siegler et al. (1994) found that severe kidney or neurological impairments (end stage renal disease or stroke) occurred in 9 (5.7%) of 157 HUS cases over a 20-year period in Utah. Using 1990 Medicare data on survival rates after kidney transplantation and survival rates on dialysis for pediatric patients, Buzby et al. (1996) estimated that approximately 60% of pediatric HUS patients who develop chronic kidney failure die prematurely.

On the basis of long-term studies in Minnesota (Martin et al. 1990) and King County, Washington (Tarr and Hickman 1987), and a 2-year, nationwide study in Canada, Rowe et al. (1991) and Mahon et al. (1997) estimated the acute mortality rate for HUS at 3% to 5%. In the study by Banatvala et al. (2001), 4 (6.5%) of 62 children with HUS died, and neither of 2 adults with HUS died. A long-term study in Utah reported 5% mortality (Siegler et al. 1994).

Occasionally, patients with *E. coli* O157:H7 are diagnosed as having TTP, a condition similar to HUS but more likely to occur in adults and with more prominent neurological findings and less renal involvement. Of 73 children and 10 adults who met the case definition for HUS in the study by Banatvala et al. (2001), 8 (11.0%) children and 8 (80.0%) adults also met the case definition for TTP. None of the children died, but 2 (25.0%) of the adults did. There are many causes of TTP other than the association with *E. coli* O157:H7, and prior to the 1980s, gastrointestinal infections had not been strongly implicated in the pathogenesis of TTP (CDC 1986). When associated with *E. coli* O157:H7 infection, TTP is probably the same disorder as HUS (Mead and Griffin 1998).

PATHOGENESIS

It is not our goal to provide a detailed review of Shiga toxin-producing *E. coli* pathogenesis, and interested readers are referred to recent publications (Paton and Paton 1998; Nataro and Kaper 1998). By definition, all STEC produce Shiga toxins; although it appears that the production of Shiga toxins is a critical factor in the pathogenesis of *E. coli* O157:H7-related disease, other important virulence factors exist as well (see below). There are two main types of Shiga toxin: Shiga toxin 1 and Shiga toxin 2. STEC strains may produce either Shiga toxin 1 or Shiga toxin 2 or both, and the genes for the toxins are encoded on lysogenic bacteriophages within the STEC chromosome. Shiga toxin 1 is almost identical to the Shiga toxin produced by *Shigella*

dysenteriae type 1, and Shiga toxin 2 is approximately 55% homologous. A second important set of virulence factors in many STEC strains is a series of genes in a 35-kilobase pathogenicity island known as the Locus for Enterocyte Effacement (LEE) (Nataro and Kaper 1998; Paton and Paton 1998). A similar pathogenicity island was first described in enteropathogenic *E.* coli (EPEC). Many of the genes within the LEE are involved in the interaction of the bacteria with the human intestinal epithelial cell barrier. For example, the *eae* gene encoded on LEE encodes a protein expressed on the bacterial surface that is critical for the close attachment of the bacteria to the host cell. Other LEE genes are involved in this bacterial docking process and in changes that occur in the host cell following bacterial interaction. Virtually all *E. coli* O157:H7 strains possess the LEE. However, some STEC strains known to be associated with HUS, such as an O113:H21 strain described in Australia (Paton et al. 1999), lack the LEE but are clearly still pathogenic. Most *E. coli* O157:H7 strains also have a 60 mega dalton plasmid that encodes enterohemolysin (hlyA), among other things. The role of the plasmid in virulence is unknown.

FACTORS AFFECTING SURVIVAL AND GROWTH OF *E. COLI* O157:H7 IN FOOD

A number of factors have a significant influence on the survival and growth of *E. coli* O157:H7 in food, including temperature, pH, salt, and water activity (Meng and Doyle 1998). Studies on the thermal sensitivity of *E. coli* O157:H7 in ground beef have revealed that the pathogen has no unusual resistance to heat and that heating ground beef sufficiently to kill typical strains of *Salmonella* will also kill *E. coli* O157:H7. Thermal pasteurization of milk has also been determined to be an effective treatment (Doyle et al. 1997). The optimal temperature for growth of *E. coli* O157:H7 is approximately 37°C (98.6°F), and the organism will not grow at temperatures below 8°C to 10°C (46°F to 50°F) or above 44°C to 45°C (Doyle and Schoeni 1984; Buchanan and Doyle 1997). *E. coli* O157:H7 survives freezing, with some decline in the concentration of *E. coli* O157:H7 (Ansay et al. 1999).

E. coli O157:H7 has been reported to be more acid resistant than other *E. coli*. Acid resistance enhances the survival of *E. coli* O157:H7 in mildly acidic foods and may explain its ability to survive passage through the stomach and cause infection at low doses. The ability to be acid resistant varies among strains and is influenced by growth phase and other environmental factors. Once induced, acid resistance is maintained for long periods of time during cold storage (Meng and Doyle 1998). Stationary-phase *E. coli* O157:H7 are more resistant than growing cells to acid (Meng and Doyle 1998). The presence of other environmental stresses, such as temperature or water activity stress, will raise the minimum pH for growth (Buchanan and Doyle 1997). *E. coli* O157:H7 survives in such foods as dry salami, apple cider, and mayonnaise, which were previously considered too acidic to support the survival of foodborne pathogens. Published literature contains conflicting reports about the efficacy of acid spray washing of beef carcasses. A study by Brachett et al. (1994) found that warm and hot acid sprays did not significantly reduce the concentration of *E. coli* O157:H7 on beef carcasses. Two recent studies have found organic acids to be effective in reducing the presence of *E. coli* O157:H7 on beef carcasses (Berry and Cutter 2000; Castillo et al. 2001). These apparently contradictory results may reflect differences in acid resistance among strains of *E. coli* O157:H7 (Berry and Cutter 2000).

E. coli O157:H7 can survive for extended periods under conditions of reduced water activity while refrigerated; however, the organism does not tolerate high salt conditions (Buchanan and Doyle 1997).

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